CHAPTER 34

Polyuria

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Polyuria can be defined as urine output exceeding 3 L/day in adults, and 2 L/m^2 in kids. Polyuria needs to be differentiated from frequency and nocturia, which are not associated with an increase in total urine output.

Causes of polyuria include glucose-induced osmotic diuresis (e.g., uncontrolled diabetes mellitus), conditions associated with a defect in water balance leading to the excretion of large volumes of diluted urine (e.g., primary/psychogenic polydipsia, central diabetes insipidus, and nephrogenic diabetes insipidus), osmotic diuresis (e.g., postobstructive diuresis, high-protein feedings, saline loading/volume expansion), prostatic hypertrophy and associated nocturia, medications (e.g., diuretics, lithium), hyperparathyroidism, and renal disease. This section focuses on selected, common causes of polyuria—other causes may be described elsewhere.

The diagnosis is often suggested through the history (age/rate of onset, family history) and by the plasma sodium concentration. In most cases the diagnosis can be confirmed by examining the response (urine volume and osmolality) to water restriction, and if appropriate, by administration of exogenous antidiuretic hormone (ADH) once plasma osmolality exceeds 295 mOsm/kg. Plasma ADH levels at baseline and post-water restriction may be helpful if the response to water restriction is equivocal.

Certain specific tests may be useful in evaluating the etiology of polyuria. These include a fasting glucose level to screen for diabetes mellitus, the exclusion of potential polyuria-inducing medication, a calcium and parathyroid hormone (PTH) level to look for hyperparathyroidism, renal functions to exclude renal diseases, a TSH to screen for hyperthyroidism, and a urine and plasma osmolality (a low urine osmolality/specific gravity and normal serum osmolality and hypernatremia point to diabetes insipidus).

DIABETES INSIPIDUS

Diabetes insipidus (DI) is an uncommon disease marked by increased thirst and passage of a large quantity of urine with a low specific gravity, usually less than 1.006. The urine is otherwise normal. The volume of ingested fluid varies from 2 to 20 L daily, with corresponding large urine volumes. Diabetes insipidus is caused by

a lack of or resistance to vasopressin. ADH deficiency causes central DI with polyuria and polydipsia; hypernatremia occurs if fluid intake is inadequate.

TYPES OF DIABETES INSIPIDUS

Primary/Central Diabetes Insipidus

If no lesion of the pituitary/hypothalamus is visible, then autoimmunity against the hypothalamic vasopressin secreting cells or genetic causes (familial DI) should be considered.

Secondary Diabetes Insipidus

Damage to the hypothalamus or pituitary stalk secondary to a tumor, anoxia, trauma, infection or metastasis may cause this to occur.

Vasopressinase–Induced Diabetes Insipidus

This occurs during the last trimester of pregnancy and puerperium. It *is* associated with oligohydramnios, preeclampsia, and hepatic dysfunction.

Nephrogenic Diabetes Insipidus

This is a defect in the renal tubules that hinders water reabsorption. The polyuria is unresponsive to vasopressin.

Symptoms

- Intense thirst, craving for ice
- Polyuria ++++
- Nocturia
- Headache
- Visual disturbance

Signs

- Hypernatremia and dehydration (if damage to hypothalamic thirst center or no access to free water)

Workup

- Clinical judgment essential
- No single lab test sufficient
- Accurate 24-hour urine collection measured for volume and creatinine (volume <2 L/24 hr in absence of hypernatremia rules out DI)
- Other screening tests
  - Fasting plasma glucose level (to rule out diabetes mellitus [DM])
  - BUN (to assess for dehydration and azotemia)
  - Calcium level (to exclude hypercalcemia, which causes polyuria)
  - Potassium level (to exclude hypokalemia, which causes polyuria)
  - Sodium level (to screen for dehydration)
  - Uric acid level (hyperuricemia can occur in patients with DI)
- Supervised vasopressin challenge test (measures urine output for 12 hours before and after administration of vasopressin; thirst and polyuria decreases and sodium stays normal in patients with central DI)

- MRI of pituitary gland/hypothalamus (to exclude mass lesions in nonfamilial DI)
- Vasopressin levels (should be elevated during modest fluid restriction in nephrogenic DI)

Comments and Treatment Considerations

Central DI post pituitary surgery may be temporary (lasting days to weeks), or permanent (if upper pituitary stalk is cut). Chronic central DI is more inconvenient than medically dangerous. Treatment with desmopressin allows normal sleep and activity. Hypernatremia can occur, especially when the thirst center is damaged, but life expectancy is not reduced, and the overall prognosis reflects that of the underlying disorder.

- Desmopressin
  - Treatment of choice for central DI
  - Also useful in pregnancy- or puerperium-related DI
  - Available in tablet form 0.05 mg twice a day to 0.4 mg three times a day; as a nasal preparation 0.05 to 0.1 mL every 12 to 24 hours; and in a parenteral form (IM, IV, subcutaneous) 1 to 4 μg every 12 to 24 hours.
  - Possible adverse reactions: nasal irritation, agitation, erythromelalgia, hyponatremia
- Mild cases of DI: adequate fluid intake may suffice
- Avoidance of aggravating factors (such as steroids) reduces polyuria.

Additional Therapies

- Hydrochlorothiazide 50 to 100 mg/day PO (with potassium supplementation) is helpful in both central and nephrogenic DI.
- Indomethacin (50 mg PO every 8 hours)—alone or in combination with hydrochlorothiazide, desmopressin or amiloride—can be effective.
- Psychotherapy is required in patients with compulsive water intake.

DIABETES MELLITUS

Increased urination arises as a consequence of osmotic diuresis secondary to sustained hyperglycemia. This results in a loss of glucose and free water and electrolytes in the urine, creating a hyperosmolar state.

Symptoms

- Polyuria ++++
- Thirst or polydipsia
- Blurred vision
- Weakness or fatigue (due to potassium loss and muscle protein catabolism)
- Paresthesias (peripheral neuropathy)
- Anorexia, nausea and vomiting (linked to ketoacidosis and hyperosmolality)
- Pruritus/vulvovaginitis

Signs

- Weight loss in spite of polyphagia (caused by the depletion of water, glucose, triglycerides, and protein) associated with random plasma glucose 200 mg/dL or more
- Fasting plasma glucose of 126 mg/dL or higher
- Nocturia
- Ketonemia, ketonuria, or both (rare in type 2 diabetes)
- Dehydration
- Postural hypotension (due to decreased plasma volume)

When an absolute insulin deficiency arises acutely, symptoms may arise abruptly (type 1 DM). Although many individuals with type 2 diabetes may present with increased urination and thirst, others may have an insidious onset of hyperglycemia and may be asymptomatic initially.

Workup

- Urine analysis for the detection of glucosuria and ketonuria
- Elevated fasting plasma glucose (normal <100; impaired glucose tolerance between 100 and 125; diabetes at or >126)
- Glycosylated hemoglobin (reflects metabolic control over 3-month period; use for screening controversial)
- Glucose tolerance test (helpful in suspected cases in which the plasma glucose <126)
- Serum fructosamine (used in cases with abnormal hemoglobins or hemolytic states)
- Fasting lipid profile
- ECG
- Renal function studies (screening for microalbuminuria)
- Evaluation of peripheral pulses
- Neurologic, podiatric, and ophthalmologic assessments

Exclusion of secondary causes of hyperglycemia (such as Cushing syndrome, medications, liver diseases, hormonal tumors, pancreatic diseases)

Comments and Treatment Considerations

- Patient education/self-management training
- Diet and weight loss
  - Carbohydrate counting (individual goal setting)
  - Cholesterol limitation (≤300 mg daily)
  - Protein intake of 10% to 20% of total calories
  - Decreased saturated fat intake (≤8% to 9% of total calories)
  - Increased dietary fiber (20 to 35 g daily)

ADA exchange lists available for meal planning (www.eatright.org)

- Oral drugs for treatment of hyperglycemia
  - Sulfonylureas, meglitinide analogs, D-phenylalanine derivates (stimulate insulin secretion)
  - Biguanides, thiazolidinediones (alter insulin action)
  - Alpha glucosidase inhibitors (affect glucose absorption)
  - Combination medications such as glyburide/metformin, rosiglitazone/metformin)
- Incretins (glucagon-like peptide analogs)

- Insulins (rapid, short, intermediate, long acting and pre-mixed preparations)

Optimal care has a marked influence on the disease prognosis, limiting complications such as microvascular disease.

Additional Therapies

- Antihypertensive management (BP goal <130/80 mm Hg)
- Treatment of dyslipidemia (LDL goal <100)
- Monitoring of renal functions and proteinuria (considering ACE-inhibitor therapy)
- Regular podiatric and ophthalmologic evaluations
- Aggressive wound care and treatment of infections such as candidiasis
- Treatment of autonomic neuropathies and erectile dysfunction
- Vaccinations (influenza, pneumovaccine)

MEDICATION-INDUCED POLYURIA

Diuretics are a common cause of polyuria. Polyuria also occurs in up to 20% of patients on chronic lithium therapy; an additional 30% have subclinical impairment in concentration ability, explained by either the decreased density of the ADH receptors or the decreased expression of aquaporin-2.

Symptoms

- Moderate polyuria ++++
- Polydipsia

Signs

- Moderate polyuria
- Polydipsia

The polyuria may be blunted by potassium administration and by once daily dosing of lithium. Nephrogenic DI may resolve about 8 weeks after cessation of lithium therapy.

Certain other medications including demeclocycline, cidofovir, foscarnet, amphotericin B, ifosfamide, ofloxacin, and orlistat can cause nephrogenic DI.

POLYURIA ASSOCIATED WITH INTERSTITIAL CYSTITIS

Patients with interstitial cystitis experience pain with bladder filling/distention, which is relieved by voiding. It is often associated with urinary urgency and frequency. Interstitial cystitis is a diagnosis of exclusion, and requires negative urine cultures as well as negative urine cytology. Other etiologies such as pelvic radiation or chemical cystitis, vaginitis, genital herpes, and urethral cancer or diverticula need to be excluded.

The majority of cases occur in women, ages 40 years and older. Fifty percent of patients experience spontaneous remissions of symptoms; the mean duration of the disease is 8 months without treatment. The exact etiology of interstitial cystitis in unknown.

It may represent several diseases with similar symptomologies. Possible causes include increased epithelial permeability, autoimmunity, and neurogenic factors. Interstitial cystitis may be associated with severe allergies, IBS, and IBD.

Symptoms
- Pain with bladder filling; relieved with urination ++++
- Urinary urgency and frequency +++
- Dyspareunia
- Urge incontinence (if bladder capacity is small)

Signs
- Frequency ++++
- Nocturia

Workup
- Urine analysis and culture to exclude infectious causes
- Urine cytology to exclude malignancy
- Urodynamic testing to assess bladder sensation and compliance, and to exclude detrussor instability
- Cystoscopy: glomerulations (submucosal hemorrhages) detected with bladder filling
- Biopsies to exclude malignancy, eosinophilic cystitis, tuberculous cystitis

Comments and Treatment Considerations
There is no specific cure for interstitial cystitis. Most patients achieve symptomatic relief from one or more of the following approaches:
- Hydrodistention (patients with a bladder capacity of <200 mL are unlikely to respond to medical therapy)
- Oxybutynin, hyoscyamine, or doxepin to decrease frequency
- Amitriptyline therapy
- Nifedipine/calcium channel blockers
- NSAIDs for pain relief and antiinflammatory effect
- Pentosan polysulfate sodium (Elmiron)—Helps restore epithelial integrity
- Intravesical instillation of dimethyl sulfoxide (DMSO), heparin, bacille Calmette-Guérin (BCG)
- Surgery (augmentation cystoplasty or cystourethrectomy with urinary diversion) as a last resort

Additional Therapies
- TENS and acupuncture may be useful. In milder cases exacerbations are followed by remissions. In severe cases, progressive disease usually requires surgery for symptom control.

References
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